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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,348	07/13/2001	Avi Ashkenazi	10466/55	3826
35489	7590	04/08/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP 275 MIDDLEFIELD ROAD MENLO PARK, CO 94025-3506			SAOUD, CHRISTINE J	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/905,348	<b>Applicant(s)</b> ASHKENAZI ET AL.	
	<b>Examiner</b> Christine J. Saoud	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 10 December 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 44-47 and 49-51 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 44-47 and 49-51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Response to Amendment***

Claims 39-43 and 48 have been cancelled and claims 44, 47 and 50 have been amended as requested in the paper 10 December 2004. Claims 44-47 and 49-51 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 10 December 2004 have been fully considered but they are not deemed to be persuasive.

### ***Claim Rejections - 35 USC § 101***

- 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 44-47 and 49-51 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons of record in the Office action mailed 29 September 2003.

Applicant argues that an assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement unless there is a reason to question the objective truth of the statement of utility or its scope. Applicant further states that the Examiner must "establish that it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility" (see page 10 of the response).

Applicant then asserts that "the working hypothesis among those skilled in the art is that, if a gene is amplified in cancer, the encoded protein is likely to be expressed at an elevated level" (see page 11 of the response). This assertion is not supported by any factual evidence and is contrary to the conclusion of Haynes et al. which indicates that protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript. Haynes' conclusions were based on a population of genes predicted to be relatively homogenous with respect to protein half-life and gene expression. Therefore, the factual data and results of Haynes et al. contradicts Applicant's unsupported assertions. Thus, the data do not support the implicit assertion that the PRO232 polypeptide can be used as a cancer diagnostic. Additionally, there is no evidence of record which indicates that the encoded protein plays any role in tumor formation and/or growth. As seen above, increased mRNA does not correlate to increased protein, and therefore, one of ordinary skill in the art would not conclude a likelihood of the protein influencing tumor formation and/or growth. Significant further research is required of the skilled artisan to determine whether PRO232 is overexpressed in any cancer to the extent that antibodies to the protein could be used as a cancer diagnostic, or if the protein influences tumor formation and/or growth to the extent that it would be a

therapeutic agent or target of therapeutic compounds, and thus the implicitly asserted utility is not substantial.

Applicant asserts at page 11 of the response that "a polypeptide encoded by a gene that is amplified in cancer would still have a specific and substantial utility". Applicant relies on the Declaration of Dr. Ashkenazi which states that "even when amplification of a cancer marker gene does not result in significant over-expression of the corresponding gene product, this very absence of gene product over-expression still provides significant information for cancer diagnosis and treatment. Thus, if over-expression of the gene product does not parallel gene amplification in certain tumor types but does so in others, then parallel monitoring of gene amplification and gene product over-expression enables more accurate tumor classification and hence better determination of suitable therapy. In addition, absence of over-expression is crucial information for the practicing clinician. If a gene is amplified but the corresponding gene product is not over-expressed, the clinician accordingly will decide not to treat a patient with agents that target that gene product.". The Declaration under 37 CFR 1.132 filed 10 December 2003 is insufficient to overcome the rejection of the claims based upon lack of utility as set forth in the last Office action because: the statements of Dr. Ashkenazi do not support a specific and substantial utility for the claimed protein in the instant application as filed. Use of the protein in the manner in which the Declaration asserts requires information which is lacking from the instant application; specifically, the expression levels of the encoded protein. Without such information, use of the protein in cancer diagnosis and treatment is not a substantial utility (i.e. a utility which

confers specific benefit to the public). . A substantial utility is a utility that defines a "real world use". Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

Claims 44-47 and 49-51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44 and 47 have been amended to recite "the amino acid sequence of the soluble domain of the polypeptide shown in Figure 9 (SEQ ID NO:18)". However, the metes and bounds of "the soluble domain" are not clear, since it would appear that the entire protein is soluble and does not contain a specific domain that is soluble to the exclusion of other portions of the protein. Therefore, Applicant's amendment has not clarified the claims, and the rejection is maintained with regard to the term "soluble".

***Priority Determination***

As the claimed subject matter is found to lack utility and enablement under 35 U.S.C. §§ 101 and 112, first paragraph, respectively, the effective priority date for this application is the instant filing date, 13 July 2001.

***Claim Rejections - 35 USC § 102***

Claims 44, 46, and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosenthal et al. (DE 19818619-A1, 28 October 1999) for the reasons of record in the Office action mailed 29 September 2003.

Applicant argues that the claimed priority of the instant application is 17 September 1997, and therefore, the rejection is not proper. This argument is not persuasive in light of the utility rejection and the effective priority of the instant application based on lack of utility.

***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTINE J. SAOUD  
PRIMARY EXAMINER

*Christine J. Saoud*